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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,478	11/17/2000	Beth Anne Allison	2196/1E500	7552

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EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/18/2001

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/715,478	ALLISON ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment to claim1 filed October 1, 2001 is acknowledged.

The outstanding rejection of claim 8 under 35 USC 112, second paragraph, is removed in view of the remarks in amendment filed October 1, 2001 regarding the term "BPD-MA" and "A-EA6" not being trademarks.

Please note that the two figures in the specification herein are not labeled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 9-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the porphyrin derivatives that are disclosed in specification page 30, line 5 – page 31, line 15 and photosensitizers at page 17, line 18 to page 35, line 15, does not reasonably provide enablement for other porphyrin derivatives or other photosensitizers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

In the instant case, there is no adequate direction or guidance provided by the applicant as to how to select any other suitable porphyrin derivatives or photosensitizers to be used in the invention to treat, prevent, inhibit or reduce restenosis or intimal hyperplasia in adjunct with angioplasty. Applicant also fails to set forth the criteria that defines neither "porphyrin derivatives or photosensitizers". Furthermore, the instant specification does not provide any working examples to show how any other porphyrin derivatives or photosensitizers besides the photosensitizers that are disclosed in specification page 17, line 18 to page 35, line 15, may be used successfully in the invention to treat, prevent, inhibit or reduce restenosis or intimal hyperplasia in adjunct with angioplasty. It is noted that these examples are neither exhaustive, nor define the class of compounds required.

Moreover, it is known in the art that different compounds may have different potency and activity because of the structural and conformational differences in the compounds. Therefore one of skilled in the art would expect a different porphyrin

derivatives other than the porphyrin derivatives that are disclosed in specification page 30, line 5 – page 31, line 15, to yield a different result. For the same reason, one of skilled in the art would also expect different photosensitizer compounds other than the photosensitizer compounds that are disclosed in specification page 17, line 18 to page 35, line 15, to yield a different result in restenosis or intimal hyperplasia. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. See MPEP 2164.03. Please note that also the instant claim reads on **all** "porphyrin derivatives or photosensitizers" compounds. Due to this unpredictability, it would prevent the skilled artisan from determining compounds which may be termed a "porphyrin derivative" or "photosensitizers" to retain the desired function of the instant invention to treat, prevent, inhibit or reduce restenosis or intimal hyperplasia in adjunct with angioplasty without undue experimentation.

Applicant's remarks filed October 1, 2001 regarding the disclosure of the instant specification enable all porphyrin derivatives because they all bearing a common feature which they all are photosensitizers have been considered but not found persuasive because the instant specification does not disclose or teach that all photosensitizers can be practiced in the instant invention. Please note that the term "photosensitizer" is broad. It is unclear what compounds are encompassed in the claims. The pharmaceutical art is unpredictable. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the instant specification only disclose a limited

number of photosensitizers applicable in the instant invention, the enablement for all photosensitizers suitable for the instant claimed invention is not seen.

Applicant's remarks filed October 1, 2001 regarding the unpredictability leading to undue experimentation not being adequately supported because the actual amount of experimentation to determine the conditions for the use of any photosensitizer requiring only routine practice of a limited number of parameters has been considered but not found persuasive because, as discussed above, predictability is only one of eight factors contributing to undue experimentation. Besides the pharmaceutical art is unpredictable, the instant specification also lacks working examples for other photosensitizers. The instant specification lists only limited number of working examples. Please note that these examples are neither exhaustive, nor define the class of compounds required. The breath of the claims are also broad, as discussed above, it reads on all photosensitizers compounds. Moreover, the amount of direction or guidance provided is not sufficient for electing a suitable photosensitizer for the use in the instant claimed invention. An exhaustive search for the embodiments suitable to practice the claimed invention is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "without depleting ... smooth muscle cells" in claim 1 renders the claims indefinite as to what method steps are required to treat or prevent intimal hyperplasia or restenosis. Please note that the prior art teaches that the result of the photodynamic therapy will deplete all cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vincent et al. (US Patent 5,422,362) in view of Adili et al. (Lasers in Surgery and Medicine 1998, 23:263-273), references of record in the previous office action mailed May 22, 2001, essential for reasons of record.

Vincent et al. teaches a method to prevent or inhibit intimal hyperplasia in adjunct with angioplasty in a subject with the administration of BPD-MA concurrent with or within 6 hours of the injury and following the angioplasty. Vincent et al. also teaches that the BPD-MA is administered to the angioplasty-injured site (See abstract; also col.10, example 1; and claims 1-22). Vincent et al. also teaches that the method is applicable to various angioplasty procedures broadly including any procedure which involves traumatic manipulation of the vasculature (See col. 3, line 62 – col. 4, line 4).

Vincent et al. also teaches the presence of smooth muscle cells after the BPD-MA therapy, i.e., without depleting all cells at the site (See particularly col. 11, line 16-19).

Vincent et al. does not expressly teach that radiation is applied in the method. Vincent et al. does not expressly teach the time to administer BPD-MA to be within 10 or 15 minutes of the angioplasty procedure.

Adili et al. teaches the use of BPD-MA in a method to inhibit Intimal hyperplasia with the use of radiation within 15 minutes of the administration of BPD-MA (See page 265, col.1 last para. to col.2, second para.).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to apply radiation onto BPD-MA in a method of inhibiting intimal hyperplasia in adjunct with angioplasty. It would have been obvious for one of ordinary skill in the art at the time the invention was made to administer BPD-MA to be within 10 or 15 minutes of the angioplasty procedure.

One of ordinary skill in the art would have been motivated to apply radiation onto BPD-MA in a method of inhibitinging, preventing or reducing intimal hyperplasia in adjunct with angioplasty because BPD-MA is known to be useful in a method of inhibiting intimal hyperplasia. Therefore, the irridiation of BPD-MA in the adjunct method of inhibiting or preventing intimal hyperplasia in Vincent et al. would have been reasonably expected to be useful in the instant intimal hyperplasia inhibition method.

Optimization of result effect parameters (dosing regimens e.g., frequency, and timing of radiation) is obvious as being within the skill of the artisan, absent evidence to the contrary.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, examples 1-2 in the specification page 42-45 have been considered but not found persuasive because the data from the examples merely demonstrate that the administration of Verteporfin (BPD-MA) and subsequent irradiation is effective in inhibiting intimal hyperplasia, this is seen to be an expected result based on the cited prior art. Further, in light of the statistical data provided for Example 2 on page 45 of the instant specification clear and convincing differences in all result data values presented are not apparent. No clear and convincing unexpected result over the closest prior art is seen.

Response to Remarks

Applicant's assertion filed October 1, 2001 that the reference of Adili et al. would destroy the teaching of Vincent et al. because Vincent et al. teaching the use of photosensitizers without the use of photoactivation have been considered but not found persuasive because even though the method of Vincent et al. does not require photoactivation or irradiation, it clearly teaches that photoactivation of photosensitizers are known to be effective in the prevention of restenosis and have been used in the past

(See Vincent et al., col. 1, line 15 to col. 3, line 22, whole column, Background Art Section). Further, Adili teaches that the preferred photosensitizer herein, BPD-MA, is known to be photoactivable in treatment to prevent intimal hyperplasia (See Adili et al. page 265, col.1 last para. to col.2, second para.).

Applicant's remarks filed October 1, 2001 regarding Adili et al. not teaching the conditions that result in the method steps of the invention as currently claimed, e.g., treating or preventing ... without depleting all endothelial and smooth muscle cells, has been considered but not found persuasive because the instant claims do not recite any method steps for the claimed method of treatment herein which are known in the prior art to result in depletion of smooth muscle cells. See page 272, col. 1, in Adili et al. which shows complete depletion of smooth muscle cells following treatment with the preferred compound herein, BPD-MA, in a manner similar to that claimed herein. Optimizing the amount of BPD-MA and the amount and type of light energy employed to be mild enough not to destroy or eradicate all the endothelial cells in the treated site is within the purview of the skilled artisan.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
December 14, 2001

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600